REMARKS/ARGUMENTS

Status of the claims

Applicants have not amended the claims in this Office Action response. Claims 54 and 55 have been canceled as being dependent on a previously canceled claim. Accordingly, claims 1-32, 37, 45-53, and 56 are pending for examination. Reconsideration is respectfully requested in light of the remarks which follow.

Claim rejections under 35 U.S.C. § 112, first paragraph - enablement

Claims 1-32, 37, 45-48, and 54-56 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement. Applicants respectfully traverse.

In order for a claim to be enabled, the specification, when filed, must contain sufficient information regarding the subject matter of the claims as to enable one skilled in the pertinent art to make and use the claimed invention without undue experimentation. *See* MPEP 2164.01. As discussed below, the specification provides more than adequate information on how to make and use the presently claimed invention without undue experimentation.

In making this rejection, the Examiner notes that in the previous Office Action response, in response to an enablement rejection, Applicants asserted that the specification provided ample evidence that an acidic amino acid containing portion, **A**, is able to prevent the uptake of a linked basic portion **B**, pointing to Examples 3-6 and Figures 7-11 of the specification to provide enablement support for the use of the term "prevent". *See* Office Action at page 3.

The Examiner has not accepted Applicants' previous arguments for enablement and has maintained the enablement rejection in the present Office Action, by alleging that "none of the peptides of Examples 3-6 and Figures 7-11 include SEQ ID NO: 1 as set forth in the amended claims". *See* Office Action at page 3. In reviewing the disclosures presented in Example 3, the Examiner states that "Applicants have shown that cellular uptake is prevented at very specific conditions", but that "independent claims 1, 11, and 46 are not limited to such conditions". *See* Office Action at page 3. Applicants respectfully disagree with the Examiner's

characterization of what the present specification teaches and whether this is reflected in the claim language.

As a preliminary matter, Applicants submit that the Examiner is in error by alleging that "none of the peptides of Examples 3-6 and figures 7-11 include SEQ ID NO: 1 as set forth in the claims". *See* Office Action at page 3. The sequence of SEQ ID NO: 1 is PLGLAG. Applicants respectfully submit that SEQ ID NO: 13 in Example 3 contains SEQ ID NO: 1 (PLGLAG) as part of its sequence.

As disclosed in the specification at page 19, paragraph [0061], the sequence PLGLAG can be used as a linker, **X**, which is cleavable by the metalloproteinase MMP-2. Example 4 and Figures 7A and 7B of the specification show that a peptide containing the sequence PLGLAG of SEQ ID NO: 1 can be efficiently cleaved by MMP-2 protease. Example 5 and Figures 11 and 12 show that the uptake of a peptide of the structure **A-X-B** (Fl) (SEQ ID NO: 13; where Fl is a fluoroscein label) into Jurkat cells is increased 10-20-fold after cleavage of the peptide at the PLGLAG linker site. Thus, as indicated in the specification, "these results demonstrate prevention of cellular uptake of compounds having basic amino acids by linkage to an acidic portion. Additionally, these results demonstrate enhanced cellular uptake of fluorescent portions of these peptides (having basic amino acids) following cleavage of the acidic portions." *See* specification at page 36, paragraph [00104].

Accordingly, Applicants respectfully disagree with the Examiner's allegation that independent claims 1, 11, and 46 do not recite the conditions described in the specification, particularly those in Examples 3-6 and their corresponding figures. Rather, the specification sets forth a molecule of the structure **A-X-B** (Fl), wherein **B** is a peptide portion of about 5 to about 20 basic amino acid residues (*e.g.*, rrrrrrrrr in SEQ ID NO: 13, among other examples), which is suitable for cellular uptake (*e.g.*, Example 5 and Figures 11 and 12 (7-6 peptide), among others), as claimed. Furthermore, as claimed, **A** is a peptide of about 2 to about 20 acidic amino acid residues (*e.g.*, eeeeee in SEQ ID NO: 13, among other examples), which when linked with portion **B** is effective to inhibit or prevent cellular uptake of portion **B** (*e.g.*, Example 5 and Figures 11 and 12 (7-6 peptide), among others). Finally, **X** is a linker of about 2 to about 100

atoms joining **A** with **B** (*i.e.*, the sequence PLGLAG contained within SEQ ID NO: 13), which can be cleaved upon physiological conditions (*e.g.*, Example 4), wherein **X** comprises the sequence of SEQ ID NO: 1 (*i.e.*, the sequence PLGLAG contained within SEQ ID NO: 13). Claim 11 further recites **C**, which is a portion comprising a cargo moiety (*e.g.*, Fl in SEQ ID NO: 13).

In addition to providing enablement for prevention of cellular uptake of peptides of the invention when the PLGLAG sequence (SEQ ID NO: 1) is used as a cleavable linker as claimed, the specification and examples contained therein describe other types of cleavable linkers that may be used. The sequence PLGLAG, as well as, other linker sequences disclosed in the present specification are well characterized cleavage sites for variety of proteases (*e.g.*, MMP-2 in the case of PLGLAG). Furthermore, because these linker sequences are provided in the context of peptides, cleavage sites within the linker sequences are readily accessible to the action of their cognate proteases under physiological conditions. Thus, the skilled artisan would be able to predictably make and use the **A-X-B** or **A-X-B-C** compositions of the present invention with no more than routine experimentation.

For the foregoing reasons, Applicants respectfully submit that the prevention of cellular uptake of the peptide compositions as claimed is amply enabled by the teachings of the specification. Accordingly, Applicants respectfully request withdrawal of this ground for rejection.

Claim rejection under obviousness-type double patenting

Claim 11 stands provisionally rejected on the grounds of nonstatutory obviousness-type double patenting as allegedly being unpatentable over claims 1, 6, and 21 of copending Application No. 11/133,804.

In the interest of expediting prosecution, Applicants respectfully request that this rejection be held in abeyance until such time as the application is otherwise deemed to be in condition for allowance. At such time, Applicants intend to provide a suitable terminal disclaimer to overcome this rejection.

Claim rejections under 35 U.S.C. § 112, second paragraph - indefiniteness

Claims 54 and 55 stand rejected under 35 U.S.C. § 112, second paragraph, as indefinite for reciting dependence upon canceled claim 39. Applicants thank the Examiner for bringing this to the attention of Applicants. Applicants have canceled claims 54 and 55, thus obviating this ground for rejection.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance and an action to that end is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,

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